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The effect of tumor necrosis factor on human sperm motility in vitro.

Eisermann J, Register KB, Strickler RC, Collins JL.

Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, Missouri 63110.

Tumor necrosis factor (TNF alpha) is present in elevated levels in peritoneal fluid from infertile women with endometriosis. The effect of TNF alpha on human sperm motility in vitro was evaluated utilizing peritoneal fluid from infertile women with minimal endometriosis containing 0, 100, 400, or 800 U of TNF alpha/ml as well as similar concentrations of recombinant human TNF alpha. No reduction in progressive and total motility was found at recombinant TNF alpha concentrations of 100 U/ml. However, 500 and 1000 U of recombinant TNF alpha/ml caused a significant reduction in progressive and total sperm motility after 4 and 21 hours of incubation when compared with controls. Similarly, peritoneal fluid containing 100 U of TNF alpha/ml did not significantly reduce progressive and total sperm motility after either 4 or 21 hours of incubation; but peritoneal fluid containing 400 U of TNF alpha/ml reduced progressive sperm motility after 4 and 21 hours and total sperm motility after 21 hours of incubation. Peritoneal fluid with a TNF alpha concentration of 800 U/ml caused a significant reduction in both progressive and total sperm motility after 4 and 21 hours when compared with controls of TNF alpha-negative peritoneal fluid. The addition of polyclonal rabbit anti-TNF alpha antibody or 30-min heat inactivation at 56 C of TNF alpha-positive peritoneal fluid reversed the inhibitory effect on sperm motility. The ability of TNF alpha to cause a significant reduction of sperm motility in vitro suggests that this may be a mechanism for the infertility observed in women with minimal endometriosis.

PMID: 2777718 [PubMed - indexed for MEDLINE]

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Gynecologic and Obstetric Investigation

**Vol. 53, Suppl. 1, 2002**[Journal Home](#)[Journal Contents](#)[Guideline](#)[Editorial](#)[Aims and
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The Fourth Japan Conference on Endometriosis
Current Perspectives on Endometriosis and Infertility
Proceedings of the Fourth Japan Conference on Endometriosis
Hakone Prince Hotel, Kanagawa, Japan, April 28, 2001
Guest Editors: H. Hoshiai, Osaka-Sayama; Y. Taketani, Tokyo; N. Terakawa,
Yonago

Session 2: Chairman: Hoshiai, H. (Osaka-Sayama). Original Article

Role of Cytokines in Endometriosis-Associated Infertility

Tomio Iwabe, Tasuku Harada, Naoki Terakawa

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Yonago, Japan

Address of Corresponding Author

Gynecologic and Obstetric Investigation 2002;53:19-25 (DOI: 10.1159/000049420)

Key Words

- Endometriosis
- Peritoneal fluid
- Interleukin-6
- Infertility

Abstract

Endometriosis, which is common in women of reproductive age, may affect fertility. It is also clear that mechanical disruption of the pelvic anatomy may cause infertility. However, our understanding of the association between the early stage of endometriosis and infertility remains incomplete. Bloody peritoneal fluid (PF) is

frequently observed in the cul-de-sac of endometriosis patients and contains various biologically active factors. We found that the concentrations of tumor necrosis factor alpha (TNF- α) and interleukin-6 (IL-6) in PF from patients with endometriosis were significantly higher than that of patients with endometriosis. There were significantly positive correlations between the levels of TNF- α and IL-6. We compared the levels of these cytokines with regard to the R-AFS stages and scores, but no differences were observed. In contrast, these cytokines correlate with the number and extent of red color peritoneal endometriosis. TNF- α increased the expression of IL-6 messenger RNA and protein in endometriotic stromal cells derived from chocolate cyst in a dose-dependent manner. The addition of IL-6 inhibited the development of mouse preimplantation embryo and impaired sperm function. We concluded that increased levels of IL-6 in peritoneal fluid of patients with active red endometriosis might be related to endometriosis-associated fertility.

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(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2002/0064826 A1**
(43) **Pub. Date:** **May 30, 2002**

(54) **CYTOKINE RECEPTOR-LIKE
POLYNUCLEOTIDES, POLYPEPTIDES, AND
ANTIBODIES**

provisional of provisional application No. 60/168,
621, filed on Dec. 3, 1999.

(76) Inventors: **Steven M. Ruben**, Olney, MD (US);
Jian Ni, Germantown, MD (US); **Paul E. Young**, Gaithersburg, MD (US);
Yanggu Shi, Gaithersburg, MD (US)

(51) **Int. Cl.⁷** **C07H 21/02; C07H 21/04;
C12P 21/02; C12N 5/06**
(52) **U.S. Cl.** **435/69.1; 435/325; 435/320.1;
536/23.1**

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(57) ABSTRACT

(21) Appl. No.: **09/874,069**

(22) Filed: **Jun. 6, 2001**

Related U.S. Application Data

(63) Continuation-in-part of application No. PCT/US00/32525, filed on Nov. 30, 2000, which is a non-

The present invention relates to novel human cytokine receptor-like polypeptides and isolated nucleic acids containing the coding regions of the genes encoding such polypeptides. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human cytokine receptor-like polypeptides. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human cytokine receptor-like polypeptides.



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Effect of cytokines on sperm motility and ionophore-stimulated acrosome reaction.

Fedder J, Ellerman-Eriksen S.

Department of Gynecology and Obstetrics, University Hospital of Aarhus, Denmark.

The effects of soluble products from leukocytes (WBC) on sperm motility and calcium ionophore-stimulated acrosome reaction (AR) were examined. Supernatants of mononuclear WBC, isolated from peripheral blood and stimulated by the lectins *Phytolacca americana* (pokeweed mitogen) or concanavalin A, caused a weak but significant inhibition of progressive sperm motility. The recombinant cytokine interferon-gamma (IFN-gamma) in high concentrations inhibited motility of sperm from 5 of 8 donors tested. The recombinant cytokines tumor necrosis factor-alpha (TNF-alpha) and interleukin-8 (IL-8) did not show any effect on sperm motility. Reactive oxygen species (ROS) produced by stimulation of polymorphonuclear WBC with a phorbol ester (PMA) tended to inhibit sperm motility. Neither supernatants from lectin-stimulated mononuclear WBC, IFN-gamma, TNF-alpha, IL-8, nor ROS showed any significant effect on the ionophore-challenged AR.

PMID: 8585773 [PubMed - indexed for MEDLINE]

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